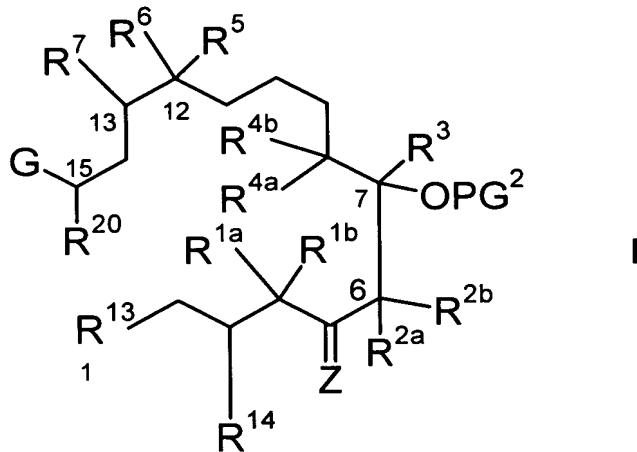


Claims

1. Process for the production of C₁-C₁₅-epothilone fragments of general formula I,



in which

R^{1a}, R^{1b} are the same or different and mean hydrogen, C₁-C₁₀-alkyl, aryl, C₇-C₂₀-aralkyl, or together mean a -(CH₂)_m group with m = 2, 3, 4 or 5,
R^{2a}, R^{2b} are the same or different and mean hydrogen, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl, C₂-C₁₀-alkynyl, aryl, C₇-C₂₀-aralkyl or together mean a -(CH₂)_n group with n = 2, 3, 4 or 5,
R³ means hydrogen, C₁-C₁₀-alkyl, aryl, C₇-C₂₀-aralkyl,
R^{4a}, R^{4b} are the same or different and mean hydrogen, C₁-C₁₀-alkyl, aryl, C₇-C₂₀-aralkyl or together mean a -(CH₂)_p group with p = 2, 3, 4 or 5,
R⁵ means hydrogen, C₁-C₁₀-alkyl, aryl, C₇-C₂₀-aralkyl,

R^6, R^7 each mean a hydrogen atom, together an additional bond or together an oxygen atom,

G means a group $X=CR^8-$, a bicyclic or tricyclic aryl radical,

R^8 means hydrogen, halogen, C_1-C_{20} -alkyl, aryl, C_7-C_{20} -aralkyl, which all can be substituted,

X means an oxygen atom, two alkoxy groups OR^{23} , a C_2-C_{10} -alkylene- α,ω -dioxy group, which can be straight-chain or branched, H/OR^9 or a grouping $CR^{10}R^{11}$,

whereby

R^{23} stands for a C_1-C_{20} -alkyl radical,

R^9 stands for hydrogen or a protective group PG^X ,

R^{10}, R^{11} are the same or different and stand for hydrogen, a C_1-C_{20} -alkyl, aryl, or C_7-C_{20} -aralkyl radical, or R^{10} and R^{11} together with the methylene carbon atom together stand for a 5- to 7-membered carbocyclic ring,

R^{13} means CH_2OR^{13a} , CH_2-Hal , CHO , CO_2R^{13b} , or $COHal$,

R^{14} means hydrogen, OR^{14a} , Hal , or OSO_2R^{14b} ,

R^{13a}, R^{14a} mean hydrogen, SO_2 -alkyl, SO_2 -aryl, SO_2 -aralkyl or together a $-(CH_2)_0$ group or together a $CR^{15a}R^{15b}$ group,

R^{13b}, R^{14b} mean hydrogen, C_1-C_{20} -alkyl, aryl, C_1-C_{20} -aralkyl,

R^{15a}, R^{15b} are the same or different and mean hydrogen, C_1-C_{10} -alkyl, aryl,

C₇-C₂₀-aralkyl, or together a -(CH₂)_q group,

o means 2 to 4,

q means 3 to 6,

R²⁰ means OPG³, NHR²⁹, or N₃,

Z means an oxygen atom or H/OR¹²,

whereby

R¹² is hydrogen or a protective group PG^Z

including all stereoisomers as well as mixtures thereof, and

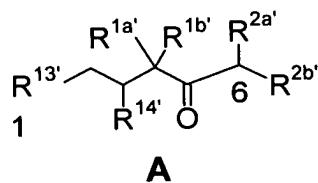
free hydroxyl groups in R¹³ and R¹⁴ can be etherified or esterified, free carbonyl

groups in Z and R¹³ can be ketalized, converted into an enol ether or reduced, and free

acid groups in R¹³ und R¹⁴ can be converted into their salts with bases,

characterized in that

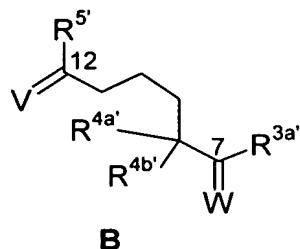
a C1-C6 fragment (epothilone numbering system) of general formula A



in which

R^{1a'}, R^{1b'}, R^{2a'}, R^{2b'}, R^{13'} and R^{14'} have the meanings already mentioned for R^{1a}, R^{1b}, R^{2a}, R^{2b}, R¹³ and R¹⁴, including all stereoisomers as well as mixtures thereof, and free hydroxyl groups in R¹³ und R¹⁴ can be etherified or esterified, free

carbonyl groups in A und R¹³ can be ketalized, converted into an enol ether or reduced, and free acid groups in A can be converted into their salts with bases, is reacted with a C7-C12 fragment (epothilone numbering system) of general formula



in which

R^{3a'}, R^{4a'}, R^{4b'} and R^{5'} have the meanings already mentioned for R^{3a}, R⁴ and

R⁵, and

V means an oxygen atom, two alkoxy groups OR¹⁷, a C₂-C₁₀-alkylene-
α,ω-dioxy group, which can be straight-chain or branched, or H/OR¹⁶,

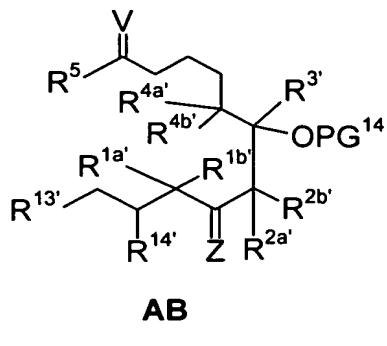
W means an oxygen atom, two alkoxy groups OR¹⁹, a C₂-C₁₀-alkylene-
α,ω-dioxy group, which can be straight-chain or branched, or H/OR¹⁸,

R¹⁶, R¹⁸, independently of one another, mean hydrogen or a protective group

PG¹,

R¹⁷, R¹⁹, independently of one another, mean C₁-C₂₀-alkyl,

to form a partial fragment of general formula AB



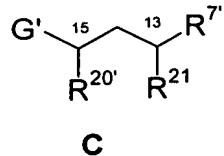
in which

R^{1a'}, R^{1b'}, R^{2a'}, R^{2b'}, R^{3'}, R^{4a'}, R^{4b'}, R⁵, R^{13'}, R^{14'}, V and Z have the already-

mentioned meanings, and

PG¹⁴ represents a hydrogen atom or a protective group PG, and

this partial fragment of general formula AB is reacted with a C13-C15 fragment
(epothilone numbering system) of general formula C



in which

G' has the meaning already mentioned in general formula I for G, and

R^{7'} means a hydrogen atom,

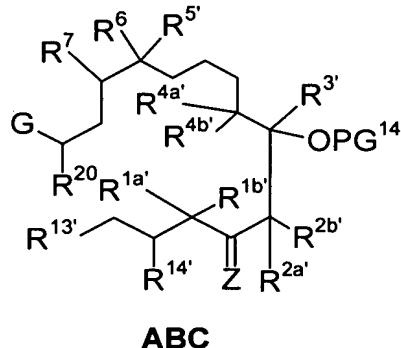
R^{20'} means halogen, N₃, NHR²⁹, a hydroxy group, a protected hydroxy group

O-PG³, a protected amino group NR²⁹PG³, a C₁-C₁₀-alkylsulfonyloxy

group, which optionally can be perfluorinated, a benzyloxy group that is optionally substituted by C₁-C₄-alkyl, nitro, chlorine or bromine, an NR²⁹SO₂CH₃ group, an NR²⁹C(=O)CH₃ group, or a CH₂-C(=O)-CH₃ group,

- R²¹ means a hydroxy group, halogen, a protected hydroxy group OPG³, a phosphonium halide radical PPh₃⁺Hal⁻ (Ph = Phenyl; Hal = F, Cl, Br, I), a phosphonate radical P(O)(OQ)₂ (Q = C₁-C₁₀-alkyl or phenyl) or a phosphine oxide radical P(O)Ph₂ (Ph = Phenyl),
- R²⁹ means hydrogen or C₁-C₆-alkyl,

to form a compound of general formula ABC (= compound of general formula I)



in which

R^{1a'}, R^{1b'}, R^{2a'}, R^{2b'}, R^{3'}, R^{4a'}, R^{4b'}, R^{5'}, R⁶, R⁷, R¹³, R¹⁴, G and Z have the already mentioned meanings, and

PG¹⁴ represents a hydrogen atom or a protective group PG.

2. Process according to claim 1, wherein a compound of general formula I,
in which

R^{1a}, R^{1b} are the same and mean C_1-C_6 -alkyl, or together mean a $-(CH_2)_m$ group

with $m = 2, 3$ or 4 ,

R^{2a}, R^{2b} are different and mean hydrogen, C_1-C_6 -alkyl, C_2-C_{10} -alkenyl,

C_2-C_{10} -alkinyl or C_7-C_{20} -aralkyl,

R^5 means hydrogen, C_1-C_6 -alkyl,

R^8 means hydrogen, halogen, C_1-C_6 -alkyl,

R^{15a}, R^{15b} are the same or different and mean hydrogen, C_1-C_6 -alkyl, aryl,

C_7-C_{20} -aralkyl, or together mean a $-(CH_2)_q$ group,

q means 3 to 6,

is produced.

3. Process according to claim 1, wherein a compound of general formula I,
in which

R^{1a}, R^{1b} are the same and mean C_1-C_3 -alkyl, or together mean a $-(CH_2)_m$ group

with $m = 2, 3$ or 4 ,

R^{2a} means hydrogen,

R^{2b} means C_1-C_5 -alkyl, C_2-C_6 -alkenyl, or C_2-C_6 -alkinyl,

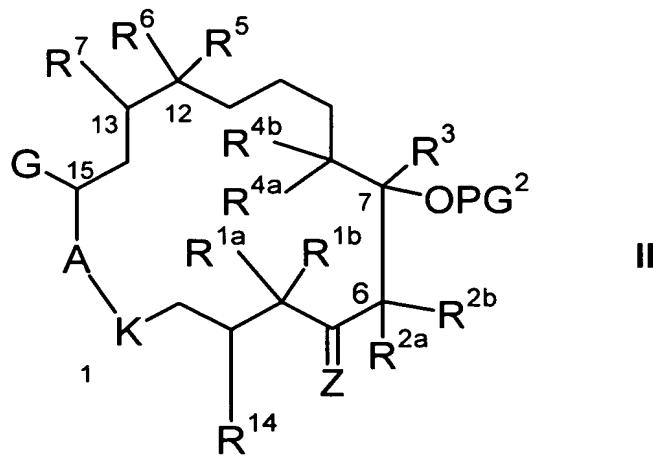
R^5 means hydrogen, or C_1-C_3 -alkyl,

R^6, R^7 together mean an additional bond,

G means a group $X=CR^8-$, or a bicyclic aryl radical,

R^8 means hydrogen, fluorine, chlorine, or C₁-C₃-alkyl,
 X means oxygen or a group CR¹⁰R¹¹,
 R^{10} means hydrogen,
 R^{11} means aryl,
 R^{13} means CH₂OR^{13a} or CO₂R^{13b},
 R^{14} means OR^{14a},
 R^{13a}, R^{14a} together mean a CR^{15a}R^{15b} group,
 R^{13b} means hydrogen or C₁-C₆-alkyl,
 R^{15a}, R^{15b} are the same and mean C₁-C₃-alkyl, or together mean a -(CH₂)_q
group, or
 R^{15a}, R^{15b} are different and mean hydrogen or aryl,
 q means 4 or 5,
 Z means oxygen,
is produced.

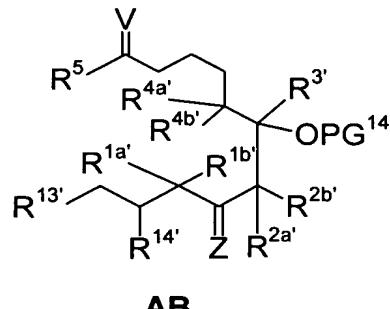
4. Process for the production of epothilone derivatives of general formula II



in which substituents R^{1a}, R^{1b}, R^{2a}, R^{2b}, R³, R^{4a}, R^{4b}, R⁵, R⁶, R⁷, G, OPG² and Z have the meanings that are indicated in general formula I, and

A–K means a group –O-C(=O), -OCH₂- , -CH₂C(=O)-, -NR²⁹-C(=O)-, or -NR²⁹-SO₂-, wherein an initial epothilone product of general formula I that is obtained according to one of the preceding claims 1 to 3 is cyclized.

5. Compounds of general formula AB



in which R^{1a'}, R^{1b'}, R^{2a'}, R^{2b'}, R³, R^{4a'}, R^{4b'}, R⁵, R^{13'}, R^{14'}, V and Z have the already mentioned meanings, and PG¹⁴ represents a hydrogen atom or a protective group PG.